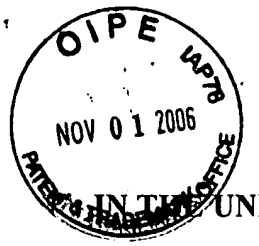

Docket No.: 20052/1200517-US3
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Randolph J. Noelle

Application No.: 09/467,317 Confirmation No.: 2231

Filed: December 20, 1999 Art Unit: 1644

For: USE OF ANTIBODIES THAT SPECIFICALLY BIND CD40CR (CD40 LIGAND) TO INHIBIT HUMORAL IMMUNITY Examiner: P. Gambel

PRE-APPEAL BRIEF REQUEST FOR REVIEW

MS AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Concurrent with the filing of a Notice of Appeal, and in accordance with the Pre-Appeal Brief Conference Program, Applicant hereby requests a pre-Appeal Brief review of the final rejection mailed May 5, 2006 in the above-identified application. No amendments are being filed with this request. With all claims having been twice rejected, an appeal is proper in accordance with 37 C.F.R. § 41.31(a).

Claims 83-86 and 90-94 are pending in this application. The sole questions on appeal are whether the Examiner is correct in rejecting the claims (a) under 35 U.S.C. § 112, first paragraph, for lack of written description; (b) under 35 U.S.C. § 112, first paragraph, for lack of enablement; (c) under 35 U.S.C. § 102(a) for anticipation by Lederman *et al.* (U.S. Patent No. 5,993,816, "Lederman"); and (d) under 35 U.S.C. § 103 as obvious over Lederman in view of Armitage *et al.* (U.S. Patent No. 5,96,974, "Armitage").

Review is being requested for the following reasons.

The Written Description Rejection under 35 U.S.C. § 112, 1st ¶, should be Withdrawn

The Examiner contends that the specification does not sufficiently describe claims 83-86 and 90-94 to reasonably convey to one of skill in the art that the inventor had possession of the invention at the time the application was filed. It is submitted that this rejection is in clear error.

One basis for the Examiner's rejection is the holding in the Federal Circuit case *Noelle v. Lederman,* finding lack of written description in a related patent. However, the claims at issue in the current application are completely different from the claims at issue in *Noelle* and thus, the case cannot be relied upon to prove that the present claims do not comply with the requirement.

The claims at issue in *Noelle* covered various forms of CD40CR antibody: mouse, human and a genus form. The Court ruled that the claims to the human and genus CD40CR antibodies were lacking in written description because only the mouse CD40CR antigen was fully characterized and adequately described in the application.

The claims at issues here cover methods of inhibiting immunoglobulin production (claims 83 and 85), or inhibiting activation of B-cells (claims 84 and 86), or treating an autoimmune condition (claim 91), comprising administering an antibody that recognizes and binds a well-characterized antigen. In contrast to the claimed CD40CR antibody claimed in *Noelle*, the antigen called for in the present claims is *fully characterized*, in part by its specific interaction with CD40-Ig, which is a fusion protein comprising the binding domain of the human CD40 protein joined to a portion of an antibody immunoglobulin chain. See specification, p. 11, l. 10-22; p. 22, l. 23 - p. 23, l. 3; Figure 8. The amino acid sequence of the human CD40 domain of CD40-Ig construct is described in the application (Figure 8). With a disclosed sequence and structure, the CD40-Ig construct is easily envisioned by one of skill in the art. Given this, one of skill in the art would recognize the inventor had possession of any antigen that binds to the CD40-Ig construct. See Amendment dated September 20, 2005, p. 6. Additionally, the specification further provides specific examples of T-cell antigens that bind CD40-Ig, such as murine CD40CR (specification, p. 28, l. 8 - p. 30, l. 35) and implicitly, human, since the CD40 portion of the CD40-Ig construct is human CD40CR, and an example of CD40-Ig binding to human T-cells (specification, p. 31, ll. 20-31; Figure 7). The claimed antigen is further described by the physical characteristic of molecular weight, and the functional characteristic of expression on activated but not resting T-cells (specification, p. 15, ll. 15-21; p. 28, l. 8 - p. 30, l. 35; Figures 3, 4, and 6). See also Amendment dated September 20, 2005, pp. 7; 13-14; Amendment after Final Action dated July 5, 2006, pp. 6-8.

The current claims also cover the use of an antibody that binds to the antigen. This antibody is also described in the specification in sufficient detail to show that the inventor had possession of the

antibody at the time of filing. The antibody is described as blocking the specific binding of CD40-Ig to activated helper T-cells. This establishes that the antibody and CD40 have overlapping or identical binding epitopes on the antigen (specification, p. 29, ll. 8-13), which is a unique characteristic of the antibody. The antibody also is described by its functional characteristic of inhibiting T-cell activation of B-cells (specification, p. 28, l. 35 - p. 29, l. 30). Not only is the antibody described in the specification, but uses of the antibody are also described (specification, p. 17, l. 10 - p. 19, l. 20). See also Amendment dated September 30, 2005, pp. 7-8;14; Amendment after Final dated July 5, 2006, pp. 7-8. Thus, as shown above, one of skill in the art reading the application as filed, would have recognized that Noelle had possession of a *method of using* the claimed *antibody* recognizing a *well-characterized antigen*, as all three limitations are fully described and supported in the specification.

The Examiner also asserts that the specification does not support a human or genus of CD40CR proteins. As shown above, the Examiner's argument is misplaced because the current claims do not cover CD40CR, but rather call for a well-characterized antigen and the antibody to which it binds. Applicant has shown that the specification provides examples of both murine and human CD40CR, and further, is not relying on the disclosure of species alone to support the claims. Instead, as shown above, the Applicant is relying upon the disclosure of relevant identifying characteristics (*e.g.*, molecular weight, sequence information, cell distribution characteristics, and ligand binding characteristics of the antigen, and antigen binding and functional characteristics of the antibody), all described in the specification as filed, to establish sufficient written description and show the Applicant was in possession of the claimed invention at the time of filing the application. See Amendment dated September 30, 2005, page 7; Amendment after Final Action dated July 5, 2006, pages 9-10. Thus, the claims meet the written description requirement under 35 U.S.C. § 112, first paragraph, and this rejection should be withdrawn.

The Enablement Rejection under 35 U.S.C. § 112, 1st ¶, should be Withdrawn

The Examiner contends that claims 83-86 and 90-94 are non-enabled as to any "antigen having the characteristics recited" in the present claims. He further contends that there is not sufficient guidance and direction for the person of skill in the art to make and use the genus of CD40CR antigen, and once again relies upon the *Noelle* to support his argument.

Applicant respectfully submits that the Examiner's reliance on the *Noelle* decision for lack of enablement is even more misplaced, as the holding in *Noelle* was not, in any way, related to enablement. The factual and legal issues are too different for the decision to be binding or even be considered in the enablement determination. See Amendment dated September 30, 2005, page 17; Amendment after Final dated July 5, 2006, pages 10-11.

The Examiner further contends that the disclosure of mouse CD40CR antigen does not enable the entire genus of CD40CR antigen. However, the present claims *do not* call for "CD40CR", instead they call for an antibody that recognizes a protein recognized by CD40-Ig. The specification discloses and exemplifies how to make and use CD40-Ig (p. 22, l. 23 - p. 23, l. 3; p. 17, l. 10 - p. 19, l. 20; p. 26, l. 15 - p. 29, l. 30), as well as providing examples of CD40-Ig- bound antigens (p. 28, l. 8 - p. 30, l. 35), and how to use the MR1 antibody to isolate and characterize the mouse antigen (p. 14, ll. 6-11; Figure 5b). Using the teachings of the specification, one of skill in the art can make CD40-Ig and use it to isolate antigens, characterize the antigens, produce the antibodies that recognize the antigens, and use the antibodies in the claimed methods, without undue experimentation. See Amendment dated September 30, 2005, pp. 16-18; Amendment after Final Action dated July 5, 2006, pp.10-11. Thus, claims 83-86 and 90-94 are fully enabled and the rejection under 35 U.S.C. § 112, first paragraph, should be withdrawn.

The Rejection under 35 U.S.C.§ 102 should be Withdrawn

The Examiner also contends that the claims are anticipated under 35 U.S.C. § 102 by Lederman. The Examiner refuses to consider the Noelle Declaration under 37 C.F.R. § 1.131 which shows prior invention because the Examiner argues the Declaration is deficient. Applicant respectfully submits this is in error.

The Examiner states that the Declaration does not aver that the invention was made in the United States. In fact, the Declaration states that the invention was reduced to practice in Applicant's laboratory at Dartmouth University. It is so well known that Dartmouth University is in New Hampshire, in the United States, one would not reasonably believe that an additional statement that the invention was reduced to practice in the United States was necessary.

Secondly, the Examiner believes that the Noelle Declaration does not support the breadth of the current claims. The Declaration shows the conception and reduction to practice of MR1 prior to the earliest priority date of the Lederman patent (Declaration of Noelle dated September 29, 2005, ¶¶ 6-12). As also shown in the Noelle Declaration, MR1 inherently possesses all the properties of the claimed antibody which binds to the claimed antigen. See Declaration of Noelle dated September 29, 2005, ¶ 11; Amendment after Final Action dated July 5, 2006, page 12.

Even if one were to accept the Examiner's argument that the Noelle Declaration does not show prior invention, Lederman does not anticipate the claims. The Examiner argues that Lederman discloses "[t]he same or nearly the same patients and endpoints" as "targeted by the same or nearly the same CD40-L-specific antibodies." See Office Action dated May 5, 2006, page 11. It is respectfully submitted that

"nearly the same" is not the proper standard for anticipation, but rather that every limitation must be "identically" found in the prior art. The Examiner has not shown this.

The general description of Lederman provides no teaching or suggestion of the invention called for in the present claims. Lederman does not teach the use of an antibody that binds to an antigen that has the same molecular weight as a protein precipitated by CD40-Ig, and is pre-cleared by precipitation with CD40-Ig. Additionally, Lederman does not teach or suggest an antibody that blocks binding of CD40-Ig to the antigen. See Amendment dated September 30, 2005, pages 18-19; Amendment after Final Action dated May 5, 2006, page 13. Thus, claims 83-86 are not anticipated by Lederman.

The Rejection Under 35 U.S.C. § 103 should be Withdrawn

The Examiner also contends the claims are obvious over Lederman in view of Armitage.

As discussed above, the Noelle Declaration establishes that the present invention was conceived prior to Lederman. Thus, Lederman should be removed as a prior art reference.

Furthermore, there is no objective basis to combine Lederman and Armitage because Lederman does not mention CD40 or CD40CR, and Armitage does not provide any more than a suggestion of an antibody. Even if the two references were combined, together they do not teach or suggest each and every limitation of the claimed invention, with a reasonable expectation of success. Specifically, the combined teachings of the references do not teach or suggest the use of an antibody that binds to an antigen that has the same molecular weight as a protein precipitated by CD40-Ig, and is pre-cleared by precipitation with CD40-Ig, or an antibody that blocks the binding of CD40-Ig to the antigen. See Amendment dated September 30, 2005, pages 20-21; Amendment after Final Action dated July 5, 2006, pages 13-14. Thus, claims 83-86 and 90-94 are not obvious.

For the reasons demonstrated above, the case should be returned to the Examiner with an indication that the application is allowable.

Dated: November 1, 2006

Respectfully submitted,

By _____

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